

Derivation and analysis of pluripotent stem cell lines with inherited TGF-b mediated disorders from donated IVF embryos and reprogrammed adult skin fibroblasts

Grant Award Details

Derivation and analysis of pluripotent stem cell lines with inherited TGF-b mediated disorders from donated IVF embryos and reprogrammed adult skin fibroblasts

Grant Type: New Cell Lines

Grant Number: RL1-00662

Investigator:

Name: Michael Longaker
Institution: Stanford University
Type: PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: Embryonic Stem Cell, iPS Cell

Award Value: \$1,406,636

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Derivation and analysis of pluripotent stem cell lines with inherited TGF- β mediated disorders from donated IVF embryos and reprogrammed adult skin fibroblasts

Public Abstract: The field of regenerative medicine revolves around the capacity of a subset of cells, called stem cells, to become the mature tissues of the adult human body. By studying stem cells, we hope to develop methods and reagents for treating disease. For instance, we hope to develop methods for making stem cells become cardiovascular cells in the lab which could then be used to rapidly screen large numbers drugs that may be used to treat cardiovascular disease. In another example, if we are able to create bone in the lab from stem cells, we may be able to help treat people with catastrophic skeletal injuries such as wounded soldiers. Until recently, the most flexible type of stem cell known was the embryonic stem cell. Embryonic stem cells are pluripotent, meaning they can give rise to all of the adult tissues. In contrast, stem cells found in the adult are considered only multipotent, in that they can only become a limited number of mature cells. For example, bone marrow stem cells can give rise to all of the components of the blood, but cannot make nerves for a spinal chord. Breakthroughs in the past couple of months have indicated that it is possible to "reprogram" adult skin cells and make them become pluripotent, like stem cells from an embryo. These new kind of cells are called "induced pluripotent cells" or iPS cells for short. This has lead to great excitement within the scientific community because it raises the possibility that we may use this technology to rapidly create pluripotent stem cells from a large host of human diseases using skin from affected individuals. However, whether the new iPS cells made from skin cells and embryonic stem cells are functionally the same in all applications remains to be seen. Our lab is in the unique position to test this hypothesis. We have derived several normal embryonic stem cell lines and are in the process of deriving iPS cells from normal skin. Furthermore, we are fortunate enough to have begun deriving a new embryonic stem cell line harboring an inherited mutation that results in severe cardiovascular and bone disease that affects more than 7,500 Californians. What's more, one of our collaborators has over the past ten years assembled a cell bank of more than 50 unique adult skin cell lines with the same inherited disease. Therefore, for our proposal, we will make new normal and disease specific iPS and embryonic stem cell lines. We will use these new stem cell lines to test whether the iPS and embryonic stem cells are truly functionally the same, by comparing them after we make them become cardiovascular and bone cells. This work will allow us to advance the field of regenerative medicine on two fronts. 1. We will perform an important comparison of iPS and embryonic stem cell lines. 2. We will compare the disease specific cells with normal cells which will help us better understand cardiovascular and bone disease and pave the way for the development of new therapies.

Statement of Benefit to California: Our proposal compares normal and disease specific pluripotent stem cells derived from embryonic and adult skin sources. This proposal will benefit the state of California and its citizens in several specific ways. First, the specific inherited disease we are studying affects approximately one in every 5,000 people worldwide. That translates into over 7,500 Californians and over 60,000 men, women and children of every race and ethnic group in the United States. By examining the characteristics of the disease specific lines, we hope to better understand the mechanisms of the disease and create assays for screening new drugs that can be used to treat people with the disease. Second, this disease is one of a broad class of cardiovascular disease, called thoracic aortic disease. An estimated 3,700 Californians are treated for thoracic aortic disease every year. Our findings may provide insight into the mechanisms underlying these diseases and other cardiovascular diseases. Third, this disease also results in skeletal defects. By studying the mechanisms of the skeletal defects, we will better understand the mechanisms of bone development, which will lead to improved applications of stem cell therapies for individuals with bone injury and disease. Finally, by providing detailed comparisons of iPS and embryonic stem cells, our work will have important ramifications for the future direction of the entire field of stem cell research and regenerative medicine.

